

Curriculum Vitae “ai fini della pubblicazione”

Thibaut DENOEL, PhD

Drug Development Chemist

Radio Pharmaceuticals - Preclinical to Phase I Translation - Organic Chemistry - Radiochemistry - Radionuclides Production - Molecular Imaging - GMP - Validation - Regulatory Affairs - Product Management - Project Management

ACADEMIC EDUCATION

15/09/2000–

30/06/2004

Licentiate in Science—Chemistry—University of Liège (BE)

Thesis: “Evaluation of the synthesis of α -fluoromethyl amino acids by phase-transfer catalysis (PTC)”, *magna cum laude*

15/09/2004–

30/06/2006

Master—Chemistry—University of Liège (BE)

Thesis: “Synthesis of lanthionine derivatives”, *magna cum laude*

01/07/2006–

03/09/2014

PhD—Chemistry—University of Liège (BE)

Dissertation: “Synthesis and biological studies of lanthionine derivatives” <https://j.mp/2OgpsyY>

15/10/2015–

14/10/2019

Post-Doc—Radiochemistry—Lausanne University Hospital (CHUV) (CH)

Clinical trial phase I: “ ^{123}I Radiolabeled 3BNC117” ClinicalTrials.gov Identifier: NCT03468582

WORK EXPERIENCE

15/10/2019–

31/12/2020

Product Manager, Swiss Nuclides GmbH, Aarau (CH)

Center for Radiopharmacy (CRP) - University Hospital Zurich (UZH)

- Radionuclide production (^{64}Cu) using a GE PETtrace 800 cyclotron at 16.5 MeV (H+)/8.4 MeV (D+)
- Design of the product synthetic routes and target material characteristics
- Lead and train employees at a site for production
- Responsible of product conformity, regulatory affairs for Marketing Authorization

15/10/2015–

14/10/2019

Radiochemist, Lausanne University Hospital (CHUV) (CH)

Departments of “Nuclear Medicine and Molecular Imaging” and of “Immunology and Allergy”

- Responsible for all aspects of radiochemistry, radiopharmacy, translational work, and regulatory affairs for the HIV-1 clinical imaging project
- Clinical trial phase I completed <https://clinicaltrials.gov/ct2/show/NCT03468582>
- Preclinical and clinical development of imaging probes: radiolabeled (^{64}Cu , ^{68}Ga , ^{89}Zr , ^{111}In , ^{123}I , ^{125}I , ^{149}Tb , ^{152}Tb , ^{161}Tb , ^{177}Lu) and fluorescent monoclonal antibodies, antibody fragments, peptides, small molecules, and biological structures
- Design, theoretical and practical analysis, precision, accuracy, robustness, and validation of novel assay methods in a quality assurance system for an injectable investigational drug product
- Collaboration with Swiss Vaccine Research Institute, Rockefeller University (USA), Ludwig Cancer Research, CERN-MEDICIS, EPFL, UZH, MGH Harvard Medical School (USA), Celldex Therapeutic (USA), Bruker (USA), Debiopharm, ULg (BE), NPL (UK), Telge Kemi (SE)
- Leading master-level trainees; training PhD-level students, QC and GMP-lab technicians
- Validation of GMP processes and analytical methods for novel drugs in a clinical trial
- Quality Assurance (QA) of antibody radio pharmaceuticals for human use in a clinical trial
- Quality Control (QC) of antibody radio pharmaceuticals for human use in a clinical trial

01/09/2004–

01/10/2015

Research Scientist, Cyclotron Research Center (CRC), Liège (BE)

Departments of “Cyclotron Research Center (GIGA-CRC)” and of “Center for Protein Engineering”

- Development of photoreactive amino acid lanthionine derivatives and peptides
- *In vitro* assay for amino acid integration in bacterial peptidoglycan, enzyme kinetics (Mpl, PBP)
- Synthesis of radioactive amino acids (^{18}F FDOPA, α - ^{18}F fluoromethylphenylalanine)
- Preparation of chiral phase-transfer catalysts for enantioselective radiochemistry
- Synthesis of cyanine dyes NHS ester (Cy2, Cy3, Cy5) for fluorescent labeling of proteins
- Validation of synthetic processes and analytical methods
- Quality Assurance (QA) of pharmaceuticals, amino acids and peptides
- Quality Control (QC) of pharmaceuticals, amino acids and peptides
- Automation of synthesis of pharmaceuticals (Zymark robot and FASTlab cassette synthesizer)

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01/04/2012–

01/05/2012

Laboratory Technician QC, Lesaffre Ingredients Services, Hombourg, (BE)

- Quality Control (QC) in a batch production process of atomized food ingredients

01/09/2011–

15/12/2011

Laboratory Technician QC, Beneo-Orafti, Oreye, (BE)

- Quality Control (QC) in a continuous production process of oligofructose and inulin

CONTINUED TRAINING (LAST 5 YEARS)

2019

- GE Cyclotron PETtrace 800 Engineer Level 1 Training (80 h), *GEMS PET Systems AB*, Uppsala (SE)
- Risk Management (40 h), *EPFL*, Lausanne (CH)
- FELASA B—Laboratory Animal Science Course Module 1 (40 h), *RESAL, UNIL*, Lausanne (CH)

2018

- FACS Course (10 h), *Flow Cytometry Facility, UNIL*, Epalinges (CH)

2017

- Interactive Course on Radiopharmacy GMP (16 h), *ESMIT Learning Centre, EANM*, Vienna (AT)
- Biacore Basics Training (12 h), *Ludwig Center for Cancer Research, UNIL*, Epalinges (CH)

2016

- Radioprotection Course (8 h), *IRA*, Lausanne (CH)
- ⁸⁹Zr-Training Course (24 h), *BV Cyclotron VU*, Amsterdam (NL)

2015

- Business Management Courses (253 h), *IFAPME*, Liège (BE)

MISCELLANEOUS

Languages

French: mother tongue – **English:** professional working proficiency – **German:** beginner

Informatics

Software: office suites (*MS Office, LaTeX*), chemistry programs (*ChemOffice, MestreNova, TopSpin*), statistic and scientific graphing (*GraphPad Prism*), HPLC programs (*Empower, Clarity*), GE interfaces (*GE FASTlab Synthesizer, GE Cyclotron PETtrace 800 Master System and Service Laptop*), scientific programming (*Python, Spyder*), OS (*Windows, DOS, Linux*), monte carlo simulation (*SRIM*), Blockchain (*Bitcoin*)

Databases: organic chemistry (*SciFinder, Beilstein/Reaxys*), nuclear physic (*TENDL, Qcalc, MIRD, NuDat*), Medical (*PubMed*), Patents (*Espacenet, Patentscope*), Regulatory (*Swissmedic, FOPH, BASEC, Kofam, EDQM, Ph. Eur., ICH, Eudralex*)

Code in C++ and python: calculation of Thick Target Yields for radionuclides production using TENDL-2019 cross section data and stopping power estimates (SRIM); weighted moving average, PID controller, negative feedback loop controller

PUBLICATIONS (FULL PAPERS)

1. *Biological evaluation of new TEM1 targeting recombinant antibodies for radioimmunotherapy: in vitro, in vivo and in silico studies.* A. D'Onofrio, L. Gano, R. Melo, F. Mendes, M. C. Oliveira, **T. Denoël**, N. Schaefer, D. Viertl, J. Fierle, G. Coukos, S. Dunn, J. O. Prior, A. Paulo. *European Journal of Pharmaceutics and Biopharmaceutics* **2021**. Accepted Article. (Impact factor: 4.604)
2. *Preclinical Evaluation and Dosimetry of [¹¹¹In]CHX-DTPA-scFv78-Fc Targeting Endosialin/Tumor Endothelial Marker 1 (TEM1).* F. Cicone, **T. Denoël**, S. Gnesin, N. Riggi, M. Irving, G. Jakka, N. Schaefer, D. Viertl, G. Coukos, J. O. Prior. *Molecular Imaging and Biology* **2020** <https://doi.org/10.1007/s11307-020-01479-8> (Impact factor: 3.341)
3. *A Robust Method for Assaying the Immunoreactive Fraction in Nonequilibrium Systems.* **T. Denoël**, L. Pedrelli, G. Pantaleo, J. O. Prior. *Pharmaceutics* **2019**, *12*, 177 <https://doi.org/10.3390/ph12040177> (Impact factor: 3.850)
4. *Internal radiation dosimetry of a ¹⁵²Tb-labeled antibody in tumor-bearing mice.* F. Cicone, S. Gnesin, **T. Denoël**, T. Stora, N. P. van der Meulen, C. Müller, C. Vermeulen, M. Benešová, U. Köster, K. Johnston, E. Amato, L. Auditore, G. Coukos, M. Stabin, N. Schaefer, D. Viertl, J. O. Prior. *EJNMMI Research* **2019**, *9*, 53 <https://doi.org/10.1186/s13550-019-0524-7> (Impact factor: 2.940)
5. *Progress in lanthionine and protected lanthionine synthesis.* **T. Denoël**, C. Lemaire, A. Luxen. *Chemistry – A European Journal* **2018**, *24*, 15421–15441 <https://doi.org/10.1002/chem.201801115> (Impact factor: 5.030)
6. *Cardiac radionuclide imaging in rodents: a review of methods, results, and factors at play.* F. Cicone, D. Viertl, A. M. Quintela Pousa, **T. Denoël**, S. Gnesin, F. Scopinaro, M.-C. Vozenin, J. O. Prior. *Frontiers in Medicine* **2017**, *4*, 35 <https://doi.org/10.3389/fmed.2017.00035> (Impact factor: 3.000)
7. *Enantioselective synthesis of α -benzylated lanthionines and related tripeptides for biological incorporation into E. coli peptidoglycan.* **T. Denoël**, A. Zervosen, C. Lemaire, G. Zaragoza, B. Joris, D. Blanot, A. Luxen. *Organic and Biomolecular Chemistry* **2014**, *12*, 9853–9863 <https://doi.org/10.1039/c4ob01476f> (Impact factor: 3.550)
8. *Stereoselective synthesis of lanthionine derivatives in aqueous solution and their incorporation into the peptidoglycan of Escherichia coli.* **T. Denoël**, A. Zervosen, T. Gerard, C. Lemaire, B. Joris, D. Blanot, A. Luxen. *Bioorganic & Medicinal Chemistry* **2014**, *22*, 4621–4628 <https://doi.org/10.1016/j.bmc.2014.07.023> (Impact factor: 2.550)
9. *Synthesis of protected α -alkyl lanthionine derivatives.* **T. Denoël**, A. Zervosen, C. Lemaire, A. Plenevaux, A. Luxen. *Tetrahedron* **2014**, *70*, 4526–4533 <https://doi.org/10.1016/j.tet.2014.05.004> (Impact factor: 2.460)

TD

10. *Les chimistes écrivent aux chimistes (chimie des encres sympathiques)*. B. André, **T. Denoël**, et al. *Bulletin de l'Association Belge des Professeurs de Physique et de Chimie* **2004**, 160, 31–59

SELECTED ABSTRACTS AT CONGRESSES

1. *¹¹¹In-PCTA-VRC07 a Radiolabeled Broadly Neutralizing Antibody For HIV Imaging in Mice*. D. Viertl, **T. Denoël**, F. Cicone, C. Müller, C. Fenwick, G. Pantaleo, J. O. Prior, oral presentation, *Annual Congress of the European Association of Nuclear Medicine* **2019**, Barcelona (ES) OP-556 <https://doi.org/10.1007/s00259-019-04486-2>
2. *Labeling of 3BNC117: a broadly neutralizing human anti-HIV antibody for clinical imaging*. **T. Denoël**, D. Viertl, M. Nussenzweig, G. Pantaleo, J. O. Prior, oral presentation, *Swiss Congress of Radiology* **2018**, Lausanne (CH) NSS107 <https://j.mp/2Mbixtg>
3. *Preclinical evaluation of a single-chain variable anti TEM-1 fragment labeled with ¹¹¹In and ¹⁵²Tb*. F. Cicone, **T. Denoël**, D. Viertl, G. Jakka, M. Irving, S. Dunn, T. Stora, N. P. van der Meulen, C. Müller, C. Vermeulen, U. Köster, K. Johnston, S. Gnesin, N. Riggi, N. Schaefer, G. Coukos, J. O. Prior, oral presentation, *Annual Congress of the European Association of Nuclear Medicine* **2017**, Vienna (AT) OP-068b <https://doi.org/10.1007/s00259-017-3822-1>
4. *New improvements in the enantioselective synthesis of 2-[¹⁸F]fluoro-L-tyrosine and 6-[¹⁸F]fluoro-L-DOPA*. L. Libert, C. Lemaire, **T. Denoël**, A. Plenevaux, J. Aerts, A. Luxen, oral presentation, *18th International Symposium on Radiopharmaceutical Sciences* **2009**, Edmonton (CA) *Journal of Labelled Compounds & Radiopharmaceuticals*, 52, S196 <https://doi.org/10.1002/jlcr.1640>
5. *Synthesis of lanthionine derivatives*. **T. Denoël**, C. Lemaire, A. Plenevaux, M. Nguyen-Distèche, B. Joris, A. Luxen, poster, *European Project Eur-Intafar General Assembly* **2007**, Grenoble (FR)

INVITED TALKS

1. *Radiochemistry of radiometals. CERN-MEDICIS-Promed Leman School on Preclinical and Clinical Imaging with Radioisotopes* **2018**, Lausanne (CH) <https://j.mp/2M9F49T>
2. *Labeling with halogens/metals and first preclinical evaluation of an anti-TEM1 antibody fragment. XXIII Congress of the International Research Group on Immuno-Scintigraphy and Therapy (IRIST)* **2016**, Lausanne (CH) <https://j.mp/2KNEObS>
3. *Pheromones and semiochemicals in animal communication: overview and chemistry. Chemistry Day at the University of Liège* **2012**, Liège (BE) <https://j.mp/2LXMJJ2>

Ai sensi degli artt. 46 e 47 del D.P.R. 445/2000 e s.m.i., consapevole delle sanzioni penali previste dall'art. 76 dello stesso D.P.R. per le ipotesi di falsità in atti e dichiarazioni mendaci, dichiaro, sotto la mia personale responsabilità, che quanto sopra riportato corrisponde a vero.

Autorizzo alla pubblicazione per ottemperare agli obblighi di pubblicità e trasparenza previsti dal D.Lgs. n. 165 del 30.03.2001 e dal D. Lgs. n. 33 del 14.3.2013;

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FIRMA

